# DRAFT

# METHIDATHION

# RISK CHARACTERIZATION DOCUMENT

## Volume IV

## Responses to Comments

**Department of Pesticide Regulation**
**California Environmental Protection Agency**

**June 2006**

# METHIDATHION
# RISK CHARACTERIZATION DOCUMENT
# RESPONSES TO COMMENTS

- Response to comments from the Air Resources Board on the Draft Methidathion Environmental Fate by Environmental Monitoring Branch/DPR.

- Response to comments from the Air Resources Board on the Draft Methidathion Risk Characterization Document by the Worker Wealth and Safety Branch/DPR.

- Response to Registrants Comments on August 5, 2005 on the Draft Methidathion Risk Characterization Document by the Worker Wealth and Safety Branch/DPR.

- Response to comments from the Air Resources Board on the Draft Methidathion Risk Characterization Document by the Medical Toxicology Branch/DPR.

- Response to Gowan's Comments Risk Characterization Document for Methidathion (Revision 1) by the Medical Toxicology Branch/DPR.

- Comments from the Air Resources Board and response from the Environmental Monitoring Branch/DPR

TO: Randy Segawa
Senior Environmental Research Scientist (Supervisor)
Environmental Monitoring Branch

FROM: Parakrama Gurusinghe, Ph.D.
Associate Environmental Research Scientist
Environmental Monitoring Branch
(916) 445-9579

DATE: November 23, 2005

SUBJECT: ENVIRONMENTAL FATE OF METHIDATHION

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I presented this information to the Pesticide Registration Evaluation Committee and the Air Resources Board. There were some comments suggesting changes in some areas of the review. Those suggestions were useful and necessary changes were effected. Given below in a table are the comments by the respective agency and the changes added to the review. The attached review includes all the changes.

If you have any questions please feel free to contact me.

Attachment

| Section | Comments | Changes |
|---|---|---|
| Title page | No comments | No change |
| Added new | Pesticide Registration Evaluation Committee (PREC) suggested to include a Table of Contents | Added a Table of Contents |
| Chemical description | No comments | No change |
| Regulation | No comments | No change |
| Use Profile | PREC reviewers suggested a comparison of 1991 vs. 2003 in:<br><br>a. Amounts of pesticide used per application<br>b. Acres applied<br>c. Application rates | Added a graph (Figure 5) to show the amounts of pesticide used in pounds per application and it's percentile use for 1991 and 2003. A table gives the 50th 90th and 95th percentile values.<br><br>Added a graph (Figure 6) to show acres applied and it's percentile values for 1991 and 2003. A table gives the three percentile values as above.<br><br>Added a graph (Figure 7) to show the rates (lbs/ac) and its percentile values for 1991 and 2003. A table gives the three percentile values as above |
| Fate and Persistence in the Aquatic Environment | PREC suggested including a data point to reflect the water temperatures at the time of application. | To Table 7, added Half-Life days values for pH 9, T 15$^0$C and pH 10, and T15$^0$C. |
| Fate and Persistence in the Atmosphere | Air Resources Board reviewers suggested considering an adjustment for calculations of methidaoxon, which appears to be overestimated. | Adjusted methidaoxon concentration values (Table 11) to account for background values reported in the Air Monitoring study (Royce et al, 1993). Adjusted methidaoxon concentration values (Table 13) to account for the background values reported in the Application Monitoring study (Royce et al, 1993). |
| References | | No change |
| Registrant Comments | No comments | No additional changes other than the ones indicated above. |

- Comments from the Air resources Board and the response from the Worker Health and Safety Branch/DPR:

TO: Joseph P. Frank, Senior Toxicologist
Worker Health and Safety Branch

FROM: Sheryl Beauvais, Staff Toxicologist (Specialist) *(original signed by S. Beauvais)*
Worker Health and Safety Branch
(916) 445-4268

DATE: November 29, 2005

SUBJECT: RESPONSE TO AIR RESOURCES BOARD COMMENTS ON DRAFT METHIDATHION RISK CHARACTERIZATION DOCUMENT

The draft Exposure Assessment Document (EAD) for methidathion prepared June 4, 2004, by the Worker Health and Safety (WHS) Branch of the Department of Pesticide Regulation (DPR) was sent to the Air Resources Board (ARB) for external peer review. ARB reviewed the EAD and sent comments in a memo dated August 2, 2005. The review was greatly appreciated, and as mentioned below resulted in at least one important change to estimates in the EAD.

This memo responds to comments 7 through 15 in that review, which address the EAD. The Environmental Monitoring Branch will respond separately to comments 1 through 6, which address the draft Environmental Fate Review (Gurusinghe, 2005).

DPR also received comments from the registrant and the Pesticide Registration and Evaluation Committee. These comments resulted in changes to how some airborne exposure estimates were calculated. Major changes include use of 95$^{th}$ percentile methidathion and methidathion oxon concentrations to calculate ambient air exposure estimates (previously, 95% tolerance limits were used), and adjustment of methidathion and methidathion oxon concentrations used to estimates bystander exposures (concentrations were multiplied by a factor of 4 to account for the fact that the monitored application, in which 45 lbs active ingredient was applied, was less than the 95$^{th}$ percentile application of 180 lbs methidathion).

**Comment 7: Include a table of contents.**

This comment recommended including a table of contents. WHS agrees and has added the table of contents to the revised draft EAD.

**Comment 8: Chemical name should be consistent with Environmental Fate Review.**

This comment recommended that both the EAD and Gurusinghe (2005) use the same chemical name for methidathion. The name has been changed in the EAD.

**Comment 9: Define "24c label."**

This comment recommended that a definition be given for "24c label." To avoid confusion for the reader, the phrase has been changed to "Special Local Needs uses (FIFRA Section 24c)," and it was noted that these uses were "approved for pest problems within all or part of California." A new table (Table 1) was added that provided details about each of the Special Local Needs uses.

**Comment 10: Vapor pressure should be consistent with Environmental Fate Review.**

This comment recommended that the EAD report the same vapor pressure as the Environmental Fate Review. Dr. Gurusinghe was consulted about this, and he confirmed that there had been a typographical error in the Environmental Fate Review, which has since been corrected. Both documents now report the same vapor pressure, $3.37 \times 10^{-6}$ mmHg at 25°C.

**Comment 11: Cite DPR for status of methidathion.**

This comment recommended that the reference cited for methidathion as a candidate toxic air contaminant be DPR rather than another agency. An open-literature article was cited (Lee *et al*., 2002), but the authors are from the Department of Health Services. In response to this recommendation, an unpublished report prepared by DPR has been cited instead (Kollman, 1995).

**Comment 12: Include methidaoxon concentrations in airborne exposure estimates.**

Methidaoxon concentrations had been omitted from in ambient air and bystander exposure estimates due to poor quality assurance in the available study. This comment recommended that methidaoxon concentrations reported by ARB be included in exposure estimates, along with a comment that actual exposures to methidaoxon might be overestimated by these data.

In response to this recommendation and more specific recommendations made by Randy Segawa of DPR, methidaoxon concentrations have been incorporated into exposure estimates. Because of the detection of methidaoxon in blanks and the fact that the lab used a gas chromatograph with an electron capture detector (ECD), which is relatively non-specific, methidaoxon concentrations were calculated after first subtracting the average methidaoxon concentration in blanks, 0.13 µg, from each individual positive sample.

**Comment 13: Resolve inconsistency in reported methidathion concentrations.**

This comment noted that the mean and standard deviation methidathion concentrations reported for the Jefferson School site differed between Table 4 and Table 11. The values reported in Table 4 are correct, and the values given in Table 11 have been changed.

**Comment 14: Resolve inconsistency in reported ambient air monitoring duration.**

On page 11 of the EAD, ambient air monitoring was stated (correctly) to have been done over a four-week period, from June 27 through July 25, 1991. However, on page 38, it was incorrectly stated to have been done over an eight-week period. The second statement has been corrected in the EAD.

**Comment 15: Include missing references.**

Two references were cited but not listed in the References section of the EAD (MacCollum *et al*., 1968; Seiber *et al*., 2003). These references have been added.

**References**

Gurusinghe, P. 2005. Environmental Fate of Methidathion. Draft document dated July 18. Sacramento, CA: California Department of Pesticide Regulation, Environmental Monitoring Branch.

Kollman, W.S. 1995. Summary of Assembly Bill 1807/3219. Pesticide Air Monitoring Results. Report No. EH 95-10. Sacramento, CA: Environmental Monitoring and Pest Management Branch, Department of Pesticide Regulation.

Lee, S., McLaughlin, R., Harnly, M., Gunier, R. and Kreuzer, R. 2002. Community exposure to airborne agricultural pesticides in California: ranking of inhalation risks. Environ. Health Perspect.110:1175-1184.

MacCollom, G.B., Johnston, D.B. and Parker, B.L. 1968. Determination and measurement of dust particles in atmospheres adjacent to orchards. Bull. Environ. Contam. Toxicol. 3:368-374.

Siebers, J., Binner, R. and Wittich, K.P. 2003. Investigation on downwind short-range transport of pesticides after application in agricultural crops. Chemosphere 51:397-407.

- Comments from the Registrant and the response from the Worker Health and Safety Branch/DPR:

TO: Joseph P. Frank, Senior Toxicologist
Worker Health and Safety Branch

FROM: Sheryl Beauvais, Staff Toxicologist (Specialist) *(original signed by S. Beauvais)*
Worker Health and Safety Branch
(916) 445-4268

DATE: November 30, 2005

SUBJECT: RESPONSE TO REGISTRANT COMMENTS ON AUGUST 5, 2005, DRAFT METHIDATHION RISK CHARACTERIZATION DOCUMENT

The draft Exposure Assessment Document (EAD) for methidathion prepared August 4, 2005, by the Worker Health and Safety (WHS) Branch of the Department of Pesticide Regulation (DPR), and the draft Risk Characterization Document (RCD) prepared August 5, 2005, were posted for public comment on the DPR website. Gowan Company provided comments on information contained in both the RCD and EAD in a memo dated October 11, 2005. This memo responds to comments in that review, which address the air monitoring data and airborne exposure estimates. The Medical Toxicology (MT) Branch will respond separately to comments about oncogenic risk.

**Comment 1: Methidathion oxon data should not be included in airborne exposure estimates.**

In the posted draft EAD, ambient air and bystander exposure estimates were provided exclusively for methidathion, due to poor quality assurance for methidathion oxon air monitoring data in the only available study. The above comment concurred with the initial DPR decision to omit these data as unreliable.

However, DPR has received additional comments about this decision from the Air Resources Board (ARB) and the Environmental Monitoring Branch of DPR, suggesting that methidathion oxon exposure should be estimated in spite of the data quality issues. In response to these recommendations, exposure estimates based on methidathion oxon concentrations have been calculated. However, because methidathion oxon was detected in blanks and because the laboratory used a relatively non-specific electron capture detector with the gas chromatograph used to analyze samples in Royce *et al.* (1993), methidathion oxon concentrations reported in the EAD were calculated after first subtracting the average methidathion oxon concentration in blanks, 0.13 µg, from each individual positive sample.

Table 1 summarizes ambient air monitoring data for methidathion and methidathion oxon; it has been modified from Table 4 of the August 4, 2005, EAD. Samples with detectable amounts of methidathion oxon have been corrected for the blank. Also, the

typographical error involving the first methidathion concentration reported at Site J has been corrected (see response below to Comment 3).

**Table 1. Methidathion Concentrations in Ambient Air Monitoring in 1991 [a]**

| Date | Site S [b] | | Site J | | Site E | | Site UC | | Site B | |
|---|---|---|---|---|---|---|---|---|---|---|
| | MT [c] | MO [c] | MT | MO | MT | MO | MT | MO | MT | MO |
| June 27 | 0.027 | *0.015* | 0.032 | *0.015* | 0.019 | *0.015* | 0.014 | 0.048 | *0.005* | *0.015* |
| July 1 | 0.024 | 0.038 | 0.018 | *0.015* | *0.005* | *0.015* | *0.005* | 0.033 | 0.013 | *0.015* |
| July 2 | *0.005* | 0.047 | 0.018 | 0.087 | 0.028 | 0.097 | *0.005* | 0.040 | 0.012 | 0.044 |
| July 3 | *0.005* | *0.015* | 0.012 | *0.015* | 0.012 | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 4 | *0.005* | *0.015* | 0.011 | *0.015* | NS [d] | NS | NS | NS | *0.005* | 0.038 |
| July 8 | *0.005* | 0.044 | *0.005* | 0.039 | *0.005* | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 9 | *0.005* | 0.061 | *0.005* | 0.037 | *0.005* | *0.015* | *0.005* | 0.055 | *0.005* | 0.033 |
| July 10 | *0.005* | 0.034 | 0.56 | 0.081 | *0.005* | *0.015* | *0.005* | *0.015* | *0.005* | 0.045 |
| July 11 | *0.005* | *0.015* | 0.30 | 0.050 | *0.005* | 0.033 | NS | NS | *0.005* | *0.015* |
| July 15 | *0.005* | *0.015* | 0.036 | *0.015* | 0.013 | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 16 | *0.005* | *0.015* | 0.023 | *0.015* | *0.005* | *0.015* | 0.010 | *0.015* | *0.005* | *0.015* |
| July 17 | *0.005* | *0.015* | 0.036 | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 18 | *0.005* | *0.015* | 0.031 | *0.015* | 0.070 | *0.015* | 0.014 | *0.015* | *0.005* | *0.015* |
| July 22 | *0.005* | *0.015* | 0.028 | *0.015* | 0.017 | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 23 | *0.005* | *0.015* | 0.025 | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* | *0.005* | *0.015* |
| July 24 | *0.005* | *0.015* | 0.015 | *0.015* | *0.005* | 0.043 | *0.005* | *0.015* | *0.005* | 0.063 |
| July 25 | *0.005* | 0.069 | 0.014 | 0.087 | *0.005* | 0.098 | 0.008 | *0.015* | *0.005* | 0.088 |
| Mean [e] | 0.011 | 0.027 | 0.069 | 0.032 | 0.013 | 0.028 | 0.007 | 0.023 | 0.006 | 0.028 |
| SD [e] | 0.009 | 0.018 | 0.144 | 0.027 | 0.017 | 0.028 | 0.003 | 0.014 | 0.002 | 0.021 |

[a] Monitoring at sites in Tulare County (Royce *et al*., 1993). Concentrations are reported in µg/m$^3$, and have not been corrected for recoveries. Methidathion oxon concentrations were corrected for the average detection in blanks of 0.13 µg/sample. For results below the limit of detection (LOD), ½ LOD was reported; these values are italicized. LOD for methidathion: 0.01 µg/m$^3$. LOD for methidathion oxon: 0.03 µg/m$^3$.

[b] Site S: Sunnyside Union Elementary School, Strathmore. Site J: Jefferson Elementary School, Lindsay. Site E: Exeter Union High School, Exeter. Site UC: University of California Lindcove Field Station, Exeter. Site B: background site at the ARB Ambient Air Monitoring Station, Visalia.

[c] MT: Methidathion. MO: Methidathion oxon.

[d] NS: No sample on this date.

[e] Arithmetic mean and standard deviation (SD).

Correction of samples with detectable amounts of methidathion oxon for the blank resulted in changes to methidathion oxon concentrations reported at all sites. Because of this, mean methidathion oxon concentrations have decreased from those reported in Table 4 of the August 4, 2005, EAD (0.031 – 0.046 µg/m$^3$) to those reported in the revised

EAD and in Table 1 of this memo (0.023 – 0.032 µg/m$^3$). In addition, more samples are reported as below the LOD.

Table 2 summarizes air monitoring done during and after an airblast application of methidathion to a 15-acre orange grove in Tulare County (Royce *et al.*, 1993); it has been modified from Table 5 of the August 4, 2005, EAD to include methidathion oxon data.

**Table 2. Methidathion Concentrations Near an Orange Grove Receiving an Application [a]**

| Date and time of monitoring | North [b] | | SE 1 [b] | | SE 2 [b] | | Wind Speed [d] | Wind Direction |
|---|---|---|---|---|---|---|---|---|
| | MT [c] | MO [c] | MT | MO | MT | MO | | |
| July 10, 1991, 1500-1600 [e] | < LOD [f] | < LOD | < LOD | < LOD | < LOD | < LOD | 5 | NW |
| July 10-11, 2330-0900 [g] | 0.33 | < LOD | < LOD | < LOD | < LOD | < LOD | 1 | SW |
| July 11, 0900-1100 | 0.86 | < LOD | < LOD | < LOD | < LOD | < LOD | 4 | SW |
| July 11, 1100-1500 | 1.40 | < LOD | < LOD | < LOD | < LOD | < LOD | 4 | W/SW |
| July 11, 1500-2130 | 0.82 | 0.16 | 1.25 | 0.18 | 0.28 | 0.16 | 3 | NW |
| 24-hour TWA [h] | 0.75 | 0.22 | 0.43 | 0.22 | 0.12 | 0.22 | NA | NA |
| July 11-12, 2130-0730 | 3.16 | 0.14 | 0.60 | < LOD | 0.10 | < LOD | 1 | SW |
| July 12-13, 0730-0730 | 0.46 | 0.18 | 0.30 | 0.14 | < LOD | < LOD | 3 | SW/NW/E/S |

[a] Concentrations reported as µg/m$^3$. Data from Royce *et al.* (1993). Concentrations are reported in µg/m$^3$, and have not been corrected for recoveries. Methidathion oxon concentrations were corrected for a blank of 0.13 µg/sample.
[b] The North station was 25 m, Southeast (SE) 1 station was 15 m, and SE 2 station was 150 m from the orchard.
[c] MT: Methidathion. MO: Methidathion oxon.
[d] Wind speed in miles/hour. NA: not applicable.
[e] Background air monitoring before application.
[f] Below limit of detection (LOD = 0.1 µg/sample for methidathion, 0.25 µg/sample for methidathion oxon).
[g] Air monitoring during application; application started at 0100 and lasted 8 hours. Subsequent measures are post-application.
[h] Time-weighted average (TWA) concentration over first 24 hours, beginning with application at 1:00 AM and ending with sample completed 9:30 PM. Samples taken during the first 20.5 hours were used as an approximation for the 24-hour TWA. For < LOD samples, ½ LOD was used in calculations. Example calculation: TWA = [(0.33 µg/m$^3$ x 8 hr) + (0.86 µg/m$^3$ x 2 hr) + (1.40 µg/m$^3$ x 4 hr) + (0.82 µg/m$^3$ x 6.5 hr)]/(20.5 hr) = 0.75 µg/m$^3$.

Table 11 of the August 4, 2005, EAD has been separated into two tables in the newly revised EAD. Table 3 summarizes ambient air exposure estimates to methidathion and methidathion oxon, based on monitoring done by Royce *et al.* (1993). Table 4 summarizes the bystander exposure estimates.

**Table 3. Ambient Air Exposure Estimates for Persons Exposed to Methidathion and Methidathion Oxon [a]**

| Site | Air concentration [b] (µg/m$^3$) Mean | SD | 95$^{th}$ percentile conc. [c] | Acute ADD [d] (mg/kg/day) Infants | Adults | Seasonal ADD [e] (mg/kg/day) Infants | Adults | Annual ADD [f] (µg/kg/day) Infants | Adults |
|---|---|---|---|---|---|---|---|---|---|
| Methidathion | | | | | | | | | |
| Site J [g] | 0.069 | 0.144 | 0.186 | 0.000110 | 0.000052 | 0.000041 | 0.000019 | 0.000031 | 0.000014 |
| Methidathion Oxon | | | | | | | | | |
| Site J [g] | 0.032 | 0.027 | 0.079 | 0.000047 | 0.000022 | 0.000019 | 0.000009 | 0.000014 | 0.000007 |

[a] Data from monitoring done in Tulare County in 1991 (Royce *et al*., 1993a).
[b] Arithmetic mean and standard deviation (SD). Calculated using ½ limit of detection (LOD) for samples < LOD.
[c] Concentration (in µg/m$^3$) used for acute exposure estimates. Calculated using lognormal distribution methods.
[d] Acute Absorbed Daily Dosage (mg/kg/day) = (95$^{th}$ percentile upper bound air concentration) x (inhalation rate). Calculation assumptions include:
- Infant inhalation rate = 0.59 m$^3$/kg/day (Layton, 1993; US EPA, 1997)
- Adult inhalation rate = 0.28 m$^3$/kg/day (Wiley *et al*., 1991; US EPA, 1997; OEHHA, 2000)
- Inhalation absorption is assumed to be 100%

[e] Seasonal ADD = (mean air concentration) x (inhalation rate). Calculation assumptions as above. Estimated season for SADD is 9 months.
[f] Annual ADD = (Seasonal ADD) x (annual use months per year)/12. Annual use estimated at 9 months.
[g] Site J = Jefferson Elementary School in Lindsay. This was the site with most samples above the LOD (see Table 4).

**Comment 2: Methidathion concentration estimates should be corrected for positive bias.**

Although most field and analytical spike recoveries were greater than 100%, DPR did not correct sample results for these recoveries. DPR does not believe that it is appropriate to adjust concentrations downward for recoveries above 100%, and does not typically do so, to minimize the likelihood of underestimating exposures calculated from these concentrations.

**Comment 3: Correct erroneous result in ambient air monitoring.**

This comment noted that the first methidathion concentration reported for Site J in Table 4 was 0.32 µg/m$^3$; it should have been 0.032 µg/m$^3$. DPR agrees this was incorrect, and has corrected the value in the EAD (see Table 1). Exposure estimates based on these data have also been revised (see Table 3).

**Table 4. Bystander Exposure Estimates for Methidathion and Methidathion Oxon [a]**

| | Adjusted Methidathion Concentration (µg/m$^3$) [b] | Adjusted Methidathion Oxon Concentration (µg/m$^3$) [b] | Inhalation Rate [c] | Absorbed Methidathion Dose [d] | Absorbed Methidathion Oxon Dose [d] |
|---|---|---|---|---|---|
| 1-Hour Absorbed Dose (during heavy activity for 1 hour) [e] | | | | | |
| Infant | 12.6 | 0.76 | 0.16 m$^3$/kg/hr | 0.00315 mg/kg/hr | 0.00019 mg/kg/hr |
| Adult | 12.6 | 0.76 | 0.022 m$^3$/kg/hr | 0.00057 mg/kg/hr | 0.000034 mg/kg/hr |
| Acute Absorbed Daily Dosage (Acute ADD) [f] | | | | | |
| Infant | 3.0 | 0.88 | 0.59 m$^3$/kg/day | 0.00177 mg/kg/day | 0.00052 mg/kg/day |
| Adult | 3.0 | 0.88 | 0.28 m$^3$/kg/day | 0.00087 mg/kg/day | 0.00026 mg/kg/day |

[a] Based on air monitoring done 25 m from a Tulare County orange grove in 1991 (Royce *et al*., 1993).

[b] Concentrations adjusted from the North station, the application air monitoring site with the highest mean methidathion and methidathion oxon concentration in the 24 hours during and post-application (see Table 2). Concentrations were multiplied by 4, the ratio between the amount of methidathion in the 95$^{th}$ percentile application (180 lbs), and 45 lbs, the amount in the application monitored by Royce *et al.* (1993).

[c] Different inhalation rates were used for the 1-hour and acute 24-hour absorbed doses. The inhalation rates for 1-hour absorbed dose estimates were calculated from values reported in Andrews and Patterson (2000), assuming heavy activity and dividing by the median body weight for males and females. Hourly inhalation rates for heavy activity are 1.9 m$^3$/hr for infants (Layton, 1993; U.S. EPA, 1997) and 3.2 m$^3$/hr for adults (Wiley *et al*., 1991; U.S. EPA, 1997; OEHHA, 2000). Daily inhalation rates are default values from Andrews and Patterson (2000).

[d] 1-hour absorbed doses assume 1-hour exposure during heavy activity, and are based on highest methidathion and methidathion oxon concentrations measured by Royce *et al*. (1993). Absorbed daily doses assume a typical mixture of activity levels throughout the day and are based on the highest 24-hour time-weighted average (TWA) air concentrations from Royce *et al.* (1993).

[e] 1-hour absorbed dose (mg/kg/hr) = (highest 1-hour air concentration) x (inhalation rate). The maximum 1-hour concentrations from Table 2 (3.16 µg/m$^3$ and 0.18 µg/m$^3$), from the North air monitoring station, were adjusted as described in Footnote [b].

[f] Acute ADD (mg/kg/day) = (TWA air concentration) x (inhalation rate). The 24-hour TWA concentrations from Table 2 (0.75 µg/m$^3$ and 0.22 µg/m$^3$), from the North air monitoring station, were adjusted as described in Footnote [b].

**Comment 4: Air monitoring samples below the limit of quantification (LOQ) should be reported as ½ LOQ, and samples below the limit of detection (LOD) should be reported as zero.**

This comment suggested that it is inappropriate to use report values for samples with non-quantifiable residues (< LOQ), or to use ½ LOD for samples with non-detectable residues
(< LOD), as was done in Table 4 and Table 5 of the August 4, 2005, EAD. DPR disagrees with this suggestion, because of the high LOQ and LOD and the fact that concentrations used in ambient air exposure estimates were based largely on samples that were above the LOD but below the LOQ. For these samples, reported values were used rather than using ½ LOQ. DPR believes that this approach is the most appropriate, as it prevents ambient air exposures from being grossly overestimated (as they might be if ½ LOQ were used for all samples below the LOQ and LOD), and also minimizes the

likelihood of exposures being underestimated (as they might be if zero were used for all samples below the LOD).

Ambient air monitoring done in 1994 (Aston and Seiber, 1997) at Site UC, one of the same sites as in 1991, provides some support for this approach. Results of monitoring done in 1994 are summarized below in Table 5, and can be compared with results of 1991 monitoring conducted at that site.

**Table 5. Methidathion Concentrations in Ambient Air Monitoring in 1994 [a]**

| Date | Site UC [b] | | Site AM | | Site K | |
|---|---|---|---|---|---|---|
| | MT [c] | MO [c] | MT | MO | MT | MO |
| May 26 | 0.015 | 0.010 | (No sample) | (No sample) | (No sample) | (No sample) |
| June 6-7 | 0.011 | 0.0085 | 0.00023 | 0.00066 | NQ | ND |
| June 20-21 | 0.0095 | 0.0082 | NQ [d] | 0.00059 | NQ | 0.00021 |
| July 11-12 | 0.0011 | 0.0023 | NQ | 0.00021 | NQ | *0.000085* |
| July 25-26 | 0.017 | 0.0093 | ND [e] | *0.000085* | NQ | ND |
| August 8-9 | 0.0024 | 0.0021 | NQ | NQ | NQ | ND |
| August 22-23 | 0.0004 | 0.001 | NQ | ND | NQ | NQ |
| September 18-19 | 0.0027 | 0.0049 | NQ | *0.000085* | NQ | ND |
| October 17-18 | 0.00058 | 0.00028 | NQ | NQ | NQ | ND |
| Mean [f] | 0.0066 | 0.0052 | 0.00023 | 0.00033 | All samples NQ | 0.00015 |
| SD [f] | 0.0066 | 0.0039 | (one sample) | 0.00028 | 0.002 | 0.000088 |

[a] Monitoring at sites in Tulare County (Aston and Seiber, 1997). Concentrations are reported in µg/m$^3$, and have not been corrected for recoveries. For results below the limit of quantification (LOQ), ½ LOQ was reported; these values are italicized. LOQ for methidathion: 0.000085 µg/m$^3$. LOQ for methidathion oxon: 0.00017 µg/m$^3$.

[b] Site UC: University of California Lindcove Field Station, Exeter, 114 m elevation. Site AM: Ash Mountain in the Sequoia National Park, 553 m elevation. Site K: Kaweah in the Sequoia National Park, 1920 m elevation.

[c] MT: Methidathion. MO: Methidathion oxon.

[d] NQ: Not quantified because duplicate samples differed by > 100%.

[e] ND: No detected: no peak detected in chromatogram.

[f] Arithmetic mean and standard deviation (SD). Site UC mean and SD for samples collected in June through July were 0.010 $\pm$ 0.0066 µg/m$^3$ for methidathion and 0.0071 $\pm$ 0.0032 µg/m$^3$ for methidathion oxon.

In 1994, methidathion concentrations at Site UC in June and July ranged 0.0095 – 0.017 µg/m$^3$ (Table 5). In 1991 monitoring done at the same site in June and July, methidathion concentrations ranged from below the LOQ to 0.014 µg/m$^3$ (Table 1). In 1994, methidathion oxon concentrations at Site UC in June and July ranged 0.0023 – 0.0085 µg/m$^3$. In 1991, methidathion oxon concentrations at the same site in June and July ranged < LOQ to 0.055 µg/m$^3$. Although the methidathion oxon concentrations reported at Site UC in 1991 are substantially higher than those reported in 1994, which might support using an approach that decreases exposure estimates, DPR does not believe this would be appropriate. For example, setting all < LOD samples to zero would result in lower exposure estimates; however, monitoring by Aston and Seiber (1997) does not support this approach. All samples from Site UC analyzed by Aston and Seiber (1997)

had detectable residues; as Site J had higher concentrations of both methidathion and methidathion oxon than Site UC (Table 1), it is even less likely that samples at Site J would have zero residues.

Studies conducted near high-use areas and with more appropriate detection limits would give better exposure estimates.

**Comment 5. Upper-bound methidathion concentration used to calculate acute ambient air exposure estimate should be calculated as 95$^{th}$ percentile rather than as an upper confidence limit on the 95$^{th}$ percentile.**

Note that the typographical error in the EAD, involving the first methidathion concentration at Site J, has been corrected from 0.32 µg/m$^3$ to 0.032 µg/m$^3$. This error had been carried through exposure calculations, and the upper-bound methidathion concentration used in the acute ambient air exposure estimate has therefore been decreased. The 95$^{th}$ percentile methidathion concentration in the revised EAD is 0.110 µg/m$^3$.

DPR agrees with this comment, and has corrected the concentrations used in estimating acute ambient air exposure to 95$^{th}$ percentile concentrations, which were calculated using lognormal methods. DPR's experience with many large environmental datasets has shown that they are usually well described by the lognormal distribution. Hence, the 95$^{th}$ percentile estimate is calculated using lognormal methods and the Site J data set reported in Table 1.

Initially, DPR calculated a 95$^{th}$ tolerance limit, which is equivalent to a 90% upper confidence limit (UCL) on the estimated percentile. DPR uses this approach for certain surrogate data sets, such as PHED. However, it is DPR policy to use 95$^{th}$ percentiles to estimate acute exposures based on chemical-specific data.

**Comment 6. Bystander exposure should be calculated based on mean exposure from all three sampling stations, rather than using concentrations from the highest.**

Because the wind was not in the direction of a sampling station during the application and for several hours afterward, it is possible that the peak concentrations were not captured; thus, exposure could have been underestimated. There is no evidence to suggest that concentrations measured at the north sampling station overestimate exposure. Averaging the concentrations across all three stations would not provide a better estimate, as it would result in decreased exposure estimates.

DPR received other comments about concentrations used to estimate bystander exposure. Specifically, comments were received that because the wind was not in the direction of a sampling station during the application and for several hours afterward, it is possible that the peak concentrations were not captured, and that the application monitored by Royce *et al.* (1993) was smaller than are many other airblast applications. In response to the first of these comments, DPR noted in the Exposure Appraisal section that bystander

exposure could have been underestimated. In response to the second comment, DPR examined amounts of methidathion applied in airblast applications, and found that the one monitored by Royce *et al.* (1993) is approximately the 70$^{th}$ percentile. The 95$^{th}$ percentile application is approximately 180 lbs AI, which is four times as large. Bystanders near a larger orchard or one receiving the maximum application rate would be anticipated to be exposed to higher concentrations than measured by Royce *et al*. (1993), and the concentrations used to estimate exposure were therefore adjusted (multiplied by 180/45 = 4). This adjustment is described in Table 4.

(see next page for references)

**References**

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- Comments from the Air Resources Board and the response from the Medical Toxicology Branch/DPR:

TO: Jim Aguila, Manager
Substance Evaluation Section
Air Quality Measures Branch
Stationary Source Division

VIA: Gary Patterson
Supervising Toxicologist
Medical Toxicology Branch

FROM: Carolyn M. Lewis
Associate Toxicologist
Medical Toxicology Branch

DATE: November 18, 2005

SUBJECT: RESPONSE TO COMMENTS FROM THE AIR RESOUCES BOARD ON DRAFT METHIDATHION RISK CHARACTERIZATION DOCUMENT

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The following response is to comments dated September 22, 2005, submitted to the Department of Pesticide Regulation by the Air Resources Board after reviewing the draft "Methidathion Risk Characterization Document" dated August 4, 2005. We found the comments useful and made the suggested minor word changes to both the Usage section in the Introduction and the Exposure Assessment section in the Risk Appraisal.

cc: Randy Segawa
Lynn Baker, Substance Evaluation Section, ARB

- Comments from the Registrant and the response from the Medical Toxicology Branch/DPR:

TO: Gary Patterson
Supervising Toxicologist
Medical Toxicology Branch

VIA: Joyce Gee
Senior Toxicologist
Medical Toxicology Branch

FROM: Carolyn M. Lewis
Associate Toxicologist
Medical Toxicology Branch

DATE: November 7, 2005

SUBJECT: RESPONSE TO GOWAN'S COMMENTS TO THE RISK CHARACTERIZATION DOCUMENT FOR METHIDATHION (REVISION 1)

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The following comments are in response to the comments from Gowan dated October 11, 2005 regarding the Risk Characterization Document (RCD) for methidathion (Revision 1). Similar comments from Gowan regarding the oncogenicity have been addressed in responses to previous drafts of the RCD and addendum; however, since more details have been presented regarding the deficiencies of several positive genotoxicity studies, a response to these comments appears warranted. Responses to comments related to air monitoring data and exposure estimates will be provided by Worker Health and Safety Branch who responsible for the Exposure Assessment Document (EAD) for methidathion.

## 1. LOW DOSE LINEAR EXTRAPOLATION IS INAPPROPRIATE

Many of the deficiencies that Gowan noted with the two positive genotoxicity studies for methidathion are probably correct. In fact, in the Genotoxicity section of the Toxicology Profile it was noted that these studies were of questionable quality given the limited information provided. This was not mentioned in the Weight of Evidence discussion of these studies and was added. However, it should be noted that because a study is not a guideline study does not mean it is not scientifically valid. All evidence, regardless of quality is considered in the weight of evidence. Naturally, more weight is given to studies of high quality. In the Weight-of-Evidence section the significance of these positive studies was also questioned because it is unclear what the biological significance of these particular studies would be even if conducted properly. Regardless, these few positive genotoxicity tests were not pivotal in DPR's decision to do a linear low dose

extrapolation for oncogenicity. If the genotoxicity evidence had been clearly positive, an upward adjustment would have been made to the cancer potency estimates to address the potential greater sensitivity of children during early life stages. On the other hand, if all the genotoxicity data been negative, DPR would have still performed a linear low dose extrapolation because there was no mechanistic data submitted to support a threshold mechanism. As stated under the quantitative assessment of oncogenic risks, this is consistent with U.S. EPA's Guidelines for Cancer Risk Assessment (2005) which recommend a linear approach be used as a default when "there is an absence of sufficient information on the mode of action." Despite insufficient data for a threshold mechanism, DPR calculated the risk for oncogenicity using a threshold approach in the Risk Appraisal section as part of the uncertainty in the oncogenicity risk estimate. U.S. EPA's 2005 Guidelines for Cancer Risk Assessment suggest using benchmark dose (BMD) analysis when evaluating oncogenicity with a threshold mechanism. The difficulty in using this threshold approach is U.S. EPA did not recommend what benchmark response (BMR) level to use for threshold carcinogens or what MOE would be considered adequate. In DPR's Benchmark Dose guidelines[1], it recommends using a BMD of 1% for endpoints that are severe. Although nongenotoxic oncogenic effects are not specifically mentioned, they could fall under pronounced pathological changes with organ dysfunction and/or long-term sequelae. The $BMDL_{01}$ for liver tumors in male mice is 0.906 mg/kg/day which would result in MOEs of 26,000 and 53,000 for children and adults, respectively. Assuming an MOE of 100 is adequate for threshold tumors, these MOEs would not trigger listing methidathion as a TAC because they were greater than 1,000. On the other hand, Gaylor et al. (1999) suggested that an MOE of 10,000 could be considered adequate when based on irreversible, nongenotoxic oncogenic effects (assuming an $BMDL_{10}$ = LOEL so UF of 10 for LOEL to NOEL extrapolation, 10 for interspecies extrapolation, 10 for intraspecies extrapolation and 10 for the severity and irreversibility of cancer). Gaylor *et al.* also recommended using the interspecies scaling factor of $BW^{3/4}$ in addition to using an interspecies UF of 10. Using this interspecies scaling factor, the $BMDL_{10}$ for liver tumors in male mice was 0.425 mg/kg/day. The MOEs for methidathion in ambient air would then be 12,000 and 25,000 for children and adults, respectively, based on this $BMDL_{10}$. Since the MOEs are not greater than 100,000, methidathion would have still be listed as a TAC using this approach.

## 2. AIR MONITORING DATA AND RISK ASSESSMENTS

### Oncogenic Risks

Gowan appears to place great importance on the fact that the highest air concentrations were found on the roof of a school. While it is unlikely that someone would spend a lifetime on the roof of a school, this site could have easily been someone's house assuming this school was located in a residential area. Although not the norm, someone could theoretically live in the same house for a lifetime. It should be noted that the air concentration that was used to calculate the oncogenic risk at this site is an average value

[1] DPR, 2004. Guidance for Benchmark Dose (BMD) Approach – Quantal Data. Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency. September 2004. DPR MT-1.

for this site, assuming the seasonal average air concentration for 9 months of the year and no exposure the remaining 3 months. In assessing the potential oncogenic risk based on somewhat limited monitoring data at a few sites, there is also no assurance that this site typified the locations having the highest concentration of methidathion in the region or the entire state. Whether there was any difference in the air concentrations of methidathion (higher or lower) at roof level compared to ground level is unknown. Without additional information, one has to assume they are the same. Even if the air concentrations were higher on the roof, someone could be exposed to similar concentrations if they lived in a two-story house. It is also possible that indoor air concentrations are lower than outdoor air concentrations, but, there is evidence for both higher and lower indoor air concentrations with pesticides which Lee *et al.* (2002) cited. Gowan states that the public policy approach to evaluate oncogenic risk is to base it on a per capita mean exposure. Although it appears Lee *et al.* (2002) from CDHS chose to average the air concentrations from all the monitoring sites to get an average air concentration, it has never been a stated policy of DPR's to do so when evaluating either occupational or ambient air exposure. It also does not appear to be the policy of U.S. EPA based on their 2005 cancer guidelines.